Public Comment

RIN#0919-AG38 ("Tobacco Products" Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act – Final Rule)

Submitted to the Office of Information and Regulatory Affairs
November 20, 2015

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I. Background

The Tobacco Vapor Electronic Cigarette Association (TVECA) has obtained a copy of the FDA electronic cigarette deeming regulations that were sent to the Office of Management and Budget (OMB) for final approval before promulgation, as well as a draft of the guidance that the agency intends to release in conjunction with the deeming regulations. The guidance relates to the recommended procedure for filing pre-market tobacco product applications (PMTA's). The TVECA has made the PMTA guidance publicly available on its web site, but did not make the deeming regulations available upon the request of the FDA.

The following commentary is based on my review of the PMTA draft guidance document. Although I have not yet reviewed the actual deeming regulations, it is possible, from analyzing the guidance, to infer the basic approach that the FDA has decided to take regarding the regulation of electronic cigarettes and vaping products. The approach the FDA is taking appears clear from the draft guidance.

Caveat: This commentary is based solely on my review of the PMTA draft guidance. It is possible, although unlikely, that the actual deeming regulations include exemptions or modified provisions for certain small businesses. I had originally made a decision to postpone my commentary on the draft guidance document until the deeming regulations were released in their entirety, in order to avoid any error in case there are exemptions in the deeming regulations. However, I have made the decision to comment now because by the time the deeming regulations are released, it will be too late to change them. I believe that the risks associated with the possibility that the fine details of the deeming regulations render invalid my commentary below are far outweighed by the benefits of making this information available to the Office of Information and Regulatory Affairs (OIRA) public so that it can conduct a fully informed review of the regulations.

II. Analysis of the FDA's Regulatory Approach

It is clear from the guidance that the approach the FDA is taking is as follows:

1. All electronic cigarette products that are sold directly to consumers (including e-liquids and vaping devices) will be required to submit a pre-market tobacco application which must be approved by the FDA in order for the product to stay on the market (it can remain on the market pending review of the application). The FDA has decided to use February 15, 2007 as the grandfather date for these regulations, and since no product currently on the market can be deemed "substantially equivalent" to products on the market eight years ago, all products will have to submit a PMTA. Products that are sold to wholesalers and retailers (i.e., not offered for sale directly to consumers) will not be required to submit a PMTA.

2. The PMTA must demonstrate that the product in question is beneficial to the public's health, taking into account not only the effects on smokers who use the product, but also the impact on nonsmokers - especially youth - who might initiate use of the product.

3. While a single PMTA may be submitted for multiple products, the demonstration in #2 must be made for every product individually. Different flavorings and different nicotine strengths constitute separate products. Thus, if a vape shop sells 100 flavors of e-liquids which it mixes itself, and each is offered at four levels of nicotine, that shop will have to demonstrate for each of the 400 products that offering it for sale to the public will benefit the public's health. All of the requirements which I describe below apply to each separate e-liquid.

4. Vaping devices are also considered tobacco products. Thus, if a company offers for sale 20 different types of vaping devices, it will have to demonstrate for each device that offering it for sale will benefit the public's health. All of the requirements which I describe below apply to each separate device.

5. The PMTA should include the following information (this is just a partial list of the most cumbersome aspects of the application):

In general, for each product (meaning each flavoring/strength combination):

- research findings on the health effects of the product;
- research findings on the effect of the product on tobacco use among users of the product;
- research findings on the effect of the product on tobacco use initiation among youth; and
- research findings on the impact of the product on the population as a whole.

Specifically, for each product:

- a complete laboratory analysis of the constituents of the aerosol, with quantification of the concentrations of at least 29 specific chemicals;
- the health risks of the product compared to never using a tobacco product;
- the likelihood of youth initiating tobacco use with the new product;
- the likelihood of former smokers re-initiating tobacco use with the new product;
- the likelihood that consumers who initiate use of the product will later switch to more hazardous tobacco products;
- the likelihood that consumers will use the product along with other tobacco products;
- the likelihood of smokers switching to the product instead of quitting completely or trying to quit with an FDA-approved medication; and

- a discussion explaining how the data above demonstrate that the introduction of the product into the market will contribute to the protection of the public's health.

And furthermore:

- For the laboratory testing, at least 10 samples from three different batches need to be tested;
- The testing must be done under a variety of conditions of use, such as varying voltages, and under conditions of intense and non-intense use;
- If a vaping device is the product in question, it must be tested with a range of e-liquids;
- If an e-liquid is the product in question, it must be tested with a range of vaping devices;
- For e-liquids and vaping devices, the shelf life must be determined under varying conditions of temperature and moisture;
- Changes in the aerosol flow rate and the constituents of the aerosol need to be tested over the life span of the e-liquid or vaping device;
- All existing studies on the safety and use of the product must be submitted, including the results of all clinical and non-clinical investigations;
- For any clinical studies of the product, the study sponsor must obtain an IND (investigational new drug) prior to initiating the research;
- In general, non-clinical studies are not enough to support the conclusion that a product is appropriate for the protection of the public's health - clinical studies of each product are generally necessary;
- For each product, genotoxicity and cytotoxicity studies are recommended;
- A thorough literature review should be conducted;
- The toxicological profile of each aerosol constituent should be provided - if no information is already available, toxicology studies need to be conducted;
- For each constituent of the aerosol, the particle size in the aerosol should be determined, as well as the deposition of through inhalation;
- For each constituent, the implications of the particle size and deposition during inhalation should be analyzed in terms of potential toxicity;
- Animal testing may be necessary to determine potential toxicity;
- For each aerosol constituent, the health effects of that chemical should be studied - both changes in physiological measurements and laboratory values (such as inflammatory markers) should be investigated;
- If there are no existing data on the toxicity of a particular chemical component of the aerosol, then computation modeling studies should be conducted using surrogate (i.e., similar) chemical structures;
- Consumer perception studies are highly recommended;
- Studies of the potential use of the product by nonsmokers (including youth) and existing smokers is highly recommended. Such studies must be related to the product itself or a similar product. Thus, an open-system vaping device could not submit information on the results of a study involving a first-generation cig-a-like product, and vice versa; and
- Puff topography studies should be included in the application.

6. In terms of the communications and marketing that will be allowed regarding electronic cigarettes and vaping products:

- E-cigarette companies and businesses will **not** be allowed to market these products for smoking cessation; and
- Therefore, no smoking cessation claims will be allowed for any of these products.

III. Implications of the FDA's Regulatory Approach

1. The most important implication of the FDA's regulatory approach for electronic cigarettes is that the FDA has apparently decided that electronic cigarettes pose a much greater threat to the health of the public than the extremely toxic tobacco cigarettes which are killing more than 400,000 Americans each year. This is evident by the fact that the agency is requiring an unduly expensive and burdensome process for every single electronic cigarette or vaping device and e-liquid to remain on the market, while the agency gave a free pass for all of the existing tobacco cigarette brands. Tobacco cigarettes can continue to kill hundreds of thousands of consumers each year with few additional restrictions or safety requirements, while the much, much safer electronic cigarettes must go through a nearly impossible, expensive, and burdensome application process.

2. The successful submission of a PMTA will be nearly impossible. In order to submit a successful application, one must demonstrate the overall benefits of your product outweigh any risks, including the possible initiation of nicotine use by nonsmokers or former smokers. One must identify the individual and population-level benefits and risks and have a mechanism to model these effects over time in order to determine and quantify the net effect on the population's long-term health. However, in the tobacco control community, there exists no consensus on any **one** aspect of the potential benefits and risks. For example, some tobacco control scientists have argued that e-cigarettes impede smoking cessation, while others (myself included) have argued that e-cigarettes aid smoking cessation. With this degree of disagreement **within** the public health community, how is a manufacturer possibly expected to wade through the quagmire in order to provide a **demonstration** of net public health benefits or risks? If scientists with 30 or more years of experience in tobacco control cannot agree upon even the individual benefits of e-cigarettes, how can a vape shop owner possibly be expected to demonstrate the long-term health consequences of allowing his particular e-cigarette product onto the market?

Moreover, there is no existing model to weigh potential risks and benefits, even if they could be quantified. For example, suppose a product could demonstrate a 15% rate of smoking cessation using the product, but that comes at the expense of 3% of youth initiating nicotine use with that product, of which 32.6% of the youth progress to cigarette smoking. How do you calculate and then weigh the risks and benefits? Is this going to result in a positive or negative net long-term public health benefit? This is an exceedingly complex question. If researchers with 30 years of experience in modeling health risks associated with changes in smoking policies cannot provide an answer, how can we expect a vape shop owner to provide the answer?

3. Putting together a PMTA will be prohibitively expensive and resource-intensive for all but the largest companies. Suppose a vape shop sells 100 flavors of self-mixed e-liquid, and each comes at three nicotine levels. That vape shop owner is going to have to submit 300 PMTAs, each one demonstrating the toxicological properties, vapor constituents, health effects, consumer use, vaping topography, risk of youth initiation, and overall risk benefit ratio for that product. The time alone required to assemble the application is itself prohibitive, but when you consider the cost of just doing the laboratory analyses, no vape shop in the country is going to be able to afford it.

4. The regulations will result in the decimation of the e-cigarette industry and put thousands of e-cigarette entrepreneurs and shops out of business. There will be a major contraction of the industry as only the tobacco companies and perhaps the largest of the independent e-cigarette companies will be able to survive the burdensome regulatory process. In the long-term, these regulations will cause e-cigarette sales to plateau, ending the possibility that vaping devices could transform the nicotine market

by creating a major shift from combustible tobacco products to much safer forms of nicotine delivery. This will be destructive to the public's health, both in the short- and long-term.

5. The regulations will create a monstrous bureaucracy, tying up thousands of hours of FDA time that could be better used to confront the smoking epidemic, which actually would save lives. Moreover, the creation of this bureaucracy will not directly protect the public's health. Instead, the FDA should have simply promulgated a set of uniform safety standards and regulations that would have immediately protected the public's health, putting an immediate end to battery explosions and other problems. These standards should have included basic quality control requirements, battery safety, and temperature/voltage regulation to prevent the formation of hazardous degradation products such as formaldehyde.

6. The regulations will essentially force the e-cigarette companies and businesses to lie to their customers by hiding from them the fact that these products were originally designed to help people quit smoking and that thousands of consumers have successfully quit smoking with these products. E-cigarette companies and businesses will not be able to communicate the truth and instead will have to rely on other "benefits" of e-cigarette use in their marketing, such as their sexiness, use by celebrities, or coolness. This marketing is much more likely to appeal to kids than truthfully informing consumers that these products were devised for the express purpose of helping people get off toxic cigarettes by providing a much safer alternative form of nicotine.

7. In reality, the requirements for a PMTA appear to be technically impossible to satisfy. While I argued above that most small businesses (e.g., vape shops) and e-cigarette companies will not be able to complete successful PMTAs because of the cost, resources, and lack of scientific expertise, it might be the case that not even the largest manufacturers - such as the tobacco companies - could be able to technically complete a successful application under the FDA deeming regulations and guidance. The studies necessary to demonstrate that the public health benefits of e-cigarettes outweigh the risks will take years. Required will be not only clinical trials of e-cigarettes to determine rates of smoking cessation, but also population-based studies to determine the rate of progression to tobacco cigarette smoking among youth who are exposed to electronic cigarettes as well as studies of the rate at which former smokers relapse to nicotine use with e-cigarettes and to cigarette smoking. Moreover, longitudinal studies will need to compare the rates of initiation or relapse with e-cigarettes with the rates that would have occurred in the absence of e-cigarettes. It's not clear to me that this can be done at all, but it certainly cannot be done within a period of 2 years (which is what the proposed deeming regulations suggested as a grace period). Even if the deeming regulations extend that grace period to 5 years, it will still not be enough time to answer all the questions that need to be addressed.

A second factor that makes the PMTA requirements technically impossible to satisfy is that a company must demonstrate the effect that marketing **its particular product** will have on the public's health, not merely the impact that the marketing of e-cigarettes **as a category** will have on the public's health. But it is technically impossible to identify the impact that marketing a particular product will have on the public's health unless the marketing of all other products was temporarily suspended. In other words, the impact of one particular product on the public's health depends not only on the marketing of that product, but on the marketing, nature, health risks, and price of all other e-cigarette or vaping products on the market.

For example, imagine that a new very-low nicotine cigarette wanted to demonstrate that it would result in a positive public health benefit. The only way such a product would likely benefit the public's health is

if all cigarettes on the market were required to be very low in nicotine. If there were alternative products on the market with higher nicotine, the low-nicotine product would be a bust, and therefore, despite any evidence of success in clinical trials, it would not improve the public's health. You simply can't demonstrate the public health impact of a single, specific product in the absence of knowing what all the products on the market are, their safety profiles, their appeal, their prices, and their effects on youth. In other words, what the companies are being asked to do in the PMTAs is **technically impossible**.

8. The deeming regulations represent a de facto prohibition of electronic cigarettes, rather than a regulatory approach to these products. I have argued for several years that the appropriate approach for the FDA to take would have been to simply promulgate a set of regulations that establish uniform manufacturing, safety, and quality control standards for electronic cigarettes. These standards could address issues such as battery safety, voltage or temperature regulation, use of known harmful flavors such as diacetyl, use of pharmaceutical grade propylene glycol, etc. That is a true **regulatory** approach.

But what the FDA is doing instead is essentially making a decision to prohibit these products, or at very least, to prohibit 99% of these products. This is not a valid regulatory approach, especially when compared to the FDA's regulatory approach for real cigarettes, which is to do nothing!

Carl Phillips provides a much more detailed and thoughtful explanation of why the FDA deeming regulations are not truly a "regulatory" approach. He writes: "Any normal use of the word [regulation] in the context of products refers to rules for product characteristics, performance standards, manufacturing standards, labeling, and the like, such that a product in the category must meet the rules to be allowed on the market. FDA's tobacco "regulation" includes almost none of that. There are some packaging and labeling rules, a ban on characteristic flavoring for cigarettes, and a prohibition against selling to minors (which is redundant with state laws). There is constant chatter about someday imposing some real regulations, like limiting quantities of particular chemicals that some believe to be independent sources of health risks, but there is nothing like that now. And there may never be, because the real effect of FDA "regulation" is simply to make it nearly impossible for manufacturers to introduce a new product or even make changes to existing products."

IV. Cost-Benefit Analysis of Regulatory Approach

These deeming regulations should really be called "The Cigarette Protection Act of 2015." They create stringent requirements for electronic cigarettes, while allowing the much more toxic real cigarettes to remain on the market, unencumbered and unchallenged by competing products that are much safer and that could have otherwise transformed the nicotine market away from combustible tobacco products, thus saving thousands of lives.

The regulations will decimate the e-cigarette industry, forcing thousands of small vapor shops and e-cigarette sellers out of business. This will no doubt result in many vapers returning to cigarette smokers and many potential quitters from trying to quit using these products.

After acknowledging that there is a continuum of risk among nicotine-containing products, with e-cigarettes at the opposite end of the spectrum from tobacco cigarettes, the FDA has chosen to ignore the risk differences and instead, to treat e-cigarettes much more stringently than tobacco cigarettes. To stay on the market, Marlboro cigarettes had to do nothing at all. But to stay on the market, much safer Vuse e-cigarettes, which have been shown to have very low emissions with non-detectable levels of all the major chemicals of concern, will have to conduct extensive research, both clinical and non-clinical studies, spending millions of dollars, in order to stay on the market for the long-term.

The regulations will also force e-cigarette companies and businesses to lie about the primary purpose and benefit of their products (an aspect of the regulations that I believe violates the free speech rights of the companies and could be successfully challenged in court).

Moreover, there is a much more cost-effective alternative available, which will protect the public's health more directly and more effectively, but at a much lower cost. The FDA should simply promulgate uniform safety standards for all electronic cigarette and vaping products. These standards should include issues such as battery safety and overcharge protection, quality assurance and control, leak-proof containers, childproof packaging, adequate regulation of temperature to avoid the production of formaldehyde and other degradation products of propylene glycol and glycerin, prohibition of flavorings known to cause human disease (e.g., diacetyl), and use of safe manufacturing practices.

Finally, the regulations do nothing to directly address the known hazards of electronic cigarettes to users, such as lack of battery safety which has resulted in battery explosions, and the presence of carcinogens like formaldehyde in the vapor which could have been prevented by setting standards for proper regulation of voltage and/or temperature.

Most importantly, while the most toxic consumer products on the market - combustible cigarettes - have to do absolutely nothing to stay on the market, much safer products such as snus and tobacco-free electronic cigarettes have to file burdensome and prohibitively expensive applications with little technical possibility of being approved under the guidance proposed by the agency.

This is an insane way to craft a regulatory strategy for the range of nicotine-containing products on the market. In fact, it is the exact opposite of the proper approach. The most toxic products - combustible cigarettes - are being given a free ride. The safest products on the market - electronic cigarettes - are being forced to complete complex, burdensome, expensive, and unruly applications for which in most cases it is technically impossible to make the demonstrations that are required by the deeming regulations.

V. Specific Violations of Executive Order 12866

The draft deeming regulations violate Executive Order 12866 in five specific ways:

1. **The regulations violate Executive Order 12866, Section 1(b)(6): "Each agency shall assess both the costs and the benefits of the intended regulation and, recognizing that some costs and benefits are difficult to quantify, propose or adopt a regulation only upon a reasoned determination that the benefits of the intended regulation justify its costs."**

   Based on my analysis, the benefits of the proposed regulations do not justify the costs. The public health benefits of the regulations are indirect and minimal. More importantly, there are delayed in time. It will take many years before the FDA can review the tens of thousands of applications that could potentially be submitted. In the meantime, urgent public health issues regarding e-cigarettes, such as exploding batteries, will continue to cause public harm.

   Moreover, FDA review of complex PMTAs does little to directly address safety issues. The regulations do not actually specify any safety standards that need to be followed.

   Furthermore, the review of PMTAs for electronic cigarettes, which are as a category far less harmful than tobacco cigarettes, serves essentially no public health purpose. In fact, the costs outweigh the benefits because the result of the regulation will be to decimate the e-cigarette industry, causing many thousands of ex-smokers to return to smoking and deterring many thousands of smokers who might have quit in the future not to do so.

   Finally, the FDA has violated section 6 of the Executive Order by failing to identify the costs of the proposed regulation in terms of the following:
   a. Effects on the potential future growth of safer nicotine delivery products to the market;
   b. The decreased availability of electronic cigarettes and vaping products to consumers;
   c. The stifling of innovation in the electronic cigarette and vaping market;
   d. The effects on ex-smokers who have quit using e-cigarettes of having their electronic cigarette brand potentially removed from the market;
   e. The effects on current smokers of removing huge numbers and types of electronic cigarettes from the market, and thus potentially dissuading them from making quit attempts using these products.

2. **The regulations violate Executive Order 12866, Section 1(b)(8): "Each agency shall identify and assess alternative forms of regulation and shall, to the extent feasible, specify performance objectives, rather than specifying the behavior or manner of compliance that regulated entities must adopt."**

   The FDA failed to identify and assess an alternative form of regulation, specifically, one which would specify performance objectives rather than requiring a complex and burdensome manner of compliance that the regulated entities must adopt. As an alternative, the FDA could have simply promulgated uniform safety standards for all electronic cigarette and vaping products. These standards could have included issues such as battery safety and overcharge protection, quality assurance and control, leak-proof containers, childproof packaging, adequate regulation of temperature to avoid the production of formaldehyde and other degradation products of

propylene glycol and glycerin, prohibition of flavorings known to cause human disease (e.g., diacetyl), and use of safe manufacturing practices.

3. **The regulations violate Executive Order 12866, Section 1(b)(5): "When an agency determines that a regulation is the best available method of achieving the regulatory objective, it shall design its regulations in the most cost-effective manner to achieve the regulatory objective."**

   The proposed regulations are far from the most cost-effective manner to achieve the regulatory objective. Far more cost-effective would have been to propose regulations which would have specified performance objectives rather than requiring a complex and burdensome manner of compliance that the regulated entities must adopt. As an alternative, the FDA could have simply promulgated uniform safety standards for all electronic cigarette and vaping products. These standards could have included issues such as battery safety and overcharge protection, quality assurance and control, leak-proof containers, childproof packaging, adequate regulation of temperature to avoid the production of formaldehyde and other degradation products of propylene glycol and glycerin, prohibition of flavorings known to cause human disease (e.g., diacetyl), and use of safe manufacturing practices.

4. **The regulations violate Executive Order 12866, section 1(b)(5): "Each agency shall tailor its regulations to impose the least burden on society, including individuals, businesses of differing sizes, and other entities (including small communities and governmental entities), consistent with obtaining the regulatory objectives, taking into account, among other things, and to the extent practicable, the costs of cumulative regulations."**

   The proposed regulations impose the most burdensome possible requirements on businesses, particular those of moderate and small size, while a much less burdensome alternative (direct regulation of vaping products via the establishment of uniform, minimum safety standards) is readily available and which would achieve the regulatory objectives not only more efficiently, but more effectively as well.

5. **The regulations violate Executive Order 12866, Section 1(b)(5): "Each agency shall draft its regulations to be simple and easy to understand, with the goal of minimizing the potential for uncertainty and litigation arising from such uncertainty."**

   The proposed regulations are about as complex as could be imagined. The process proscribed for preparing PMTAs is complex, tedious, burdensome, and scientifically complicated. It would take a group of expert scientists in multiple areas, including epidemiology, toxicology, chemistry, population modeling, statistical modeling, human behavior, communication and perception, marketing behavior, and biostatistics to understand the multitude and nature of specific studies that would be required to derive the information necessary to make the required demonstrations specified for the PMTA. The overwhelming majority of businesses that would be regulated do not have the necessary expertise to understand the regulation, much less to comply with it.

In contrast, if the agency simply set uniform safety standards, these could easily be understood by all regulated businesses.